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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,807	07/29/2002	James Duncan Morrison	9013-46	2452
28120	7590	12/14/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			AUDET, MAURY A	
			ART UNIT	PAPER NUMBER
			1654	
DATE MAILED: 12/14/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/088,807

Applicant(s)

MORRISON ET AL.

Examiner

Maury Audet

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2, 26-32, 34, 39 and 43-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 2, 26-32, 34, 39, 43-50 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 08/2004.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_.

## **DETAILED ACTION**

### ***Response to Arguments and Amendment***

Applicant's filing of an RCE on 11/26/2004 is acknowledged. Applicant's amendments to the claims, filed 10/29/2004, are also acknowledged. Claims 1, 3-25, 33, 35-38, and 40-42 have been cancelled. New claims 43-50 have been added. Claims 2, 26-32, 34, 39, and 43-50 are pending. Applicant's election of insulin as the peptide species (and correspondingly the method of use to the disease diabetes mellitus, claims 46 and 50) is maintained herein. Thus, claims 2, 26-32, 34, 39, 46, and 50, drawn to the elected species, are examined on the merits and claims 43 (calcitonin), 44 (gastrin), 45 (secretin), 47 (osteoporosis/calcitonin), 48 (secretin deficiency/secretin), and 49 (gastrin deficiency/gastrin) have been withdrawn from consideration, as not being drawn to the elected species.

### ***Invention***

Claims 2, 26-32, 34, drawn to a method of oral administration of bile acid(C-24)-peptide (insulin) conjugated compositions.

Claim 39, drawn to compositions comprising bile acid-peptide (insulin) conjugates.

Claims 46 and 50, drawn to a method of treating diabetes mellitus comprising orally administering a bile acid/insulin conjugate.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39 and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 39, it is unclear what is contemplated by term “coated” to inhibit degradation in the stomach. Applicant is asked to specifically recite the compound(s) that are added to the composition to render the composition “coated”.

Claim 46 recites the limitation "the peptide" in the last line of the claim. There is insufficient antecedent basis for this limitation in the claim. It is assumed Applicant is referring to insulin (X); however, for clarity, since insulin is the only “peptide” for which X may be, it is suggested that “the peptide” be changed to “X” or “insulin” (see i.e. claim 47).

***Claim Rejections - 35 USC § 103***

Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruff et al. (5,446,026), alone or in view of Longenecker et al. (US 4,994,439).

Ruff et al., previously discussed, teach an amide of a bile salt wherein the group bound to the bile salt by the amide bond is a calcitonin decapeptide amide (see claims 1-7). Ruff et al. further discloses pharmaceutical compositions comprising this compound for administration (claims 8-11). Ruff et al. also teach the conjugated compositions in a carrier or diluent (claim 8, i.e. reads on Applicant’s broad term “coated” of claim 39).

Longenecker et al., previously discussed, teach that “[i]t is by now well known that bile salts are capable of enhancing the absorption of peptides, such as insulin and other drugs, across the nasal mucous membrane and across the rectal and vaginal mucous membranes.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to conjugate insulin at the C-24 carboxyl group (Applicant’s claim 39, claim still drawn simply to bile acid/insulin conjugate composition) in Ruff et al., either alone, because Ruff et al. teach the advantageous binding of peptides (i.e. calcitonin) to the C-24 carboxyl group of bile acid or in view of Longenecker et al, who advantageously teach the use of insulin with bile acids for enhanced absorption.

Claims 2, 26-32, 34, 46, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Byun et al. (US 6,245,753) in view of Ruff et al. (5,446,026) and Longenecker et al. (US 4,994,439).

Byun et al., previously discussed, teach the oral administration of bile acids conjugated at the C-24 to active agents (i.e. polysaccharides, such as heparin) and uses thereof, *for enhanced oral administration and intestinal absorption*. Byun et al. also does not teach oral administration of peptides. Byun et al. does not expressly teach peptides conjugated at the C-24 of bile acids.

Longenecker et al., previously discussed and discussed above, teach that “[i]t is by now well known that bile salts are capable of enhancing the absorption of peptides, such as insulin and other drugs, across the nasal mucous membrane and across the rectal and vaginal mucous membranes.

Ruff et al., previously discussed and discussed above, teach peptides (i.e. calcitonin) conjugated to the C-24 of bile acids.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to *orally administer* peptides as the active agent of choice in Byun et al., because Longenecker et al. teach the advantageous enhancement of oral absorption of insulin by bile acids simply by the latter being in composition therewith (without the further enhancement of conjugation of the active agent as taught by Byun et al.). Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to conjugate insulin as the active agent of choice at the C-24 carboxyl group of the bile acid of Byun et al., for the reasons discussed above (1<sup>st</sup> § of 103) under either Ruff et al. alone, or Ruff et al. in view of Longenecker et al. [It is once again noted that Byun et al. teach the advantageous use of other active agents conjugated to the C-24 of bile acid to enhance mucosal absorption of active agents (*namely, polysaccharides (heparin) which Applicant had previously expressly included, among the myriad of peptides (or more aptly larger active/"pharmaceutical agents", since enzymes and hormones are included therein also), as one of the key pharmaceutical agents which may benefit through absorption assistance by conjugation to bile acids*).]

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

MA

12/09/04



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PRIMARY EXAMINER